

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

1-19. (Cancelled)

20. (Cancelled)

21-22. (Cancelled)

~~84~~ 23. (Currently amended) A method of detecting the presence or location of an IGF-IR-expressing tumor in a subject in need thereof, comprising the steps of:

a) administering the antibody or antigen-binding portion according to claim ~~34~~ or an antibody according to claim ~~39~~ or ~~46~~ to the subject; and

b) detecting binding of said antibody,

wherein said binding indicates the presence or location of the tumor.

~~85~~ 24. (Currently amended) A method of treating cancer in a human patient wherein said patient overexpresses IGF-I or IGF-IR, comprising the step of administering to the human patient an amount of the antibody or antigen-binding portion according to claim ~~34~~ effective to treat said cancer.

~~86~~ 25. (Currently amended) A method of treating a patient in need thereof, wherein said patient overexpresses IGF-I or IGF-IR, with the antibody or antigen-binding portion thereof according to claim ~~34~~, comprising the step of administering to the patient an effective amount of the antibody.

~~85~~ ~~87~~ 26. (Currently amended) The method according to either of claims claim 24 or 25, further comprising the step of administering an anti-neoplastic, anti-tumor, anti-angiogenic or chemotherapeutic agent.

27. (Cancelled)

28. (Cancelled)

29. (Cancelled)

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

30. (Cancelled)

31. (Cancelled)

32. (Cancelled)

33. (Cancelled)

34. (Currently amended) A ~~human~~ monoclonal antibody that specifically binds ~~human~~ insulin-like growth factor I receptor (IGF-IR) or an antigen-binding portion of said antibody, wherein the antibody or portion comprises the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in a variable domain selected from the group consisting of:

(a) the variable domain of the light chain of antibody 2.13.2;

and

(b) the variable domain of a light chain comprising the amino acid sequence in SEQ ID NO: 6;

~~— (c) — the variable domain of the heavy chain of antibody 2.13.2;~~

~~— (d) — the variable domain of a heavy chain comprising the amino acid sequence in SEQ ID NO: 8; and~~

~~— (e) — the variable domain of a light chain comprising SEQ ID NO: 6 and the variable domain of a heavy chain comprising SEQ ID NO: 8.~~

2 35. (Currently amended) The ~~human~~ monoclonal antibody or antigen-binding portion according to claim 34, further comprising the amino acid sequences of the heavy chain CDRs of antibody 2.13.2 and light chain CDRs of antibody 2.13.2.

3 36. (Currently amended) A monoclonal antibody or an antigen binding portion thereof that specifically binds ~~human~~ insulin-like growth factor I receptor (IGF-IR), wherein said antibody comprises a ~~variable domain of a κ light chain, and wherein~~

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

~~said variable domain of a κ light chain comprises the amino acid sequence in SEQ ID NO: 6.~~

4 37. (Currently amended) A monoclonal antibody or an antigen-binding portion thereof that specifically binds human insulin like growth factor I receptor (IGF-IR), wherein said antibody comprises ~~a variable domain of a heavy chain, and wherein said variable domain of a heavy chain comprises the amino acid sequence in SEQ ID NO: 8.~~

5 38. (Currently amended) The monoclonal antibody or antigen-binding portion according to claim 37, wherein said antibody further comprises ~~a variable domain of a light chain, and wherein said variable domain of a light chain comprises the amino acid sequence in SEQ ID NO: 6.~~

6 39. (Currently amended) A monoclonal antibody that specifically binds human insulin-like growth factor I receptor (IGF-IR), wherein said antibody comprises the amino acid sequence of the heavy chain sequence within SEQ ID NO: 45, without the signal sequence, and the amino acid sequence of the light chain sequence within SEQ ID NO: 47, without the signal sequence.

7 40. (Currently amended) A monoclonal antibody or an antigen-binding portion thereof that specifically binds human IGF-IR, comprising ~~heavy chain CDR1, CDR2 and CDR3 regions, said CDR regions comprising the CDR1, CDR2 and CDR3 amino acid sequences, respectively, in SEQ ID NO:45.~~

8 41. (Currently amended) The monoclonal antibody or antigen-binding portion according to claim 40, ~~wherein said heavy chain further comprises~~ comprising the framework amino acid sequences in SEQ ID NO: 45.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

9 ~~42~~. (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the amino acid sequence of SEQ ID NO: 45, without the signal sequence, or an antigen-binding portion of said antibody.

10 ~~43~~. (Currently amended) A monoclonal antibody or an antigen binding portion thereof that specifically binds ~~human~~ IGF-IR, comprising ~~light chain CDR1, CDR2 and CDR3 regions, said CDR regions comprising~~ the CDR1, CDR2 and CDR3 amino acid sequences, respectively, in SEQ ID NO: 47.

11 ~~44~~. (Currently amended) The monoclonal antibody or antigen-binding portion according to claim ~~43~~, wherein said ~~light chain~~ further ~~comprises~~ comprising the framework amino acid sequences in SEQ ID NO: 47.

12 ~~45~~. (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the amino acid sequence in SEQ ID NO: 47, without the signal sequence, or an antigen-binding portion of said antibody.

13 ~~46~~. (Currently amended) A monoclonal antibody that specifically binds ~~human~~ insulin-like growth factor I receptor (IGF-IR) wherein the heavy chain amino acid sequence is SEQ ID NO: 45, without the signal sequence, and the light chain amino acid sequence is SEQ ID NO: 47, without the signal sequence.

14 ~~47~~. (Previously presented) A hybridoma cell line having American Type Culture Collection (ATCC) accession number PTA-2788.

15 ~~48~~. (Currently amended) A monoclonal antibody or an antigen-binding portion thereof, that specifically binds ~~human~~ IGF-IR, comprising the heavy chain variable domain and the light chain variable domain of the antibody produced by the hybridoma cell line of claim ~~47~~.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

¹⁶/~~49~~ (Previously presented) The monoclonal antibody produced by the hybridoma cell line of claim ¹⁴/~~47~~.

¹⁷/~~50~~ (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the heavy chain amino acid sequence and the light chain amino acid sequence of the antibody produced by the hybridoma cell line having ATCC accession number PTA-2788.

¹⁸/~~51~~ (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the amino acid sequence of the heavy chain and the amino acid sequence of the light chain of antibody 2.13.2.

¹⁸/~~51~~ ¹⁹/~~52~~ (Previously presented) The monoclonal antibody according to claim ~~51~~, wherein the antibody is monoclonal antibody 2.13.2.

53. (Cancelled)

²⁰/~~54~~ (Currently amended) A monoclonal antibody or antigen-binding portion thereof that specifically binds ~~human~~ IGF-IR, comprising a heavy chain amino acid sequence that utilizes ~~the~~ human V_H3-23 gene.

55. (Cancelled)

²¹/~~56~~ (Currently amended) A monoclonal antibody or antigen-binding portion thereof that specifically binds ~~human~~ IGF-IR, comprising a light chain amino acid sequence that utilizes the human V_κ A30 gene.

²²/~~57~~ (Currently amended) The ~~human~~ monoclonal antibody or antigen-binding portion according to claim ¹/~~34~~, wherein said antibody is selected from the group consisting of: an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, a single chain antibody or a bispecific antibody.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

1 23 58. (Previously presented) The antigen-binding portion according to claim 34, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

2 24 59. (Previously presented) The antigen-binding portion according to claim 35, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

3 25 60. (Previously presented) The antigen-binding portion according to claim 36, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

4 26 61. (Previously presented) The antigen-binding portion according to claim 37, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

5 27 62. (Previously presented) The antigen-binding portion according to claim 38, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

7 28 63. (Previously presented) The antigen-binding portion according to claim 40, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

8 29 64. (Previously presented) The antigen-binding portion according to claim 41, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

9 30⁶⁵. (Previously presented) The antigen-binding portion according to claim 42, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

10 31⁶⁶. (Previously presented) The antigen-binding portion according to claim 43, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

11 32⁶⁷. (Previously presented) The antigen-binding portion according to claim 44, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

12 33⁶⁸. (Previously presented) The antigen-binding portion according to claim 45, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

15 34⁶⁹. (Previously presented) The antigen-binding portion according to claim 46, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

20 35⁷⁰. (Previously presented) The antigen-binding portion according to claim 47, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

21 36⁷¹. (Previously presented) The antigen-binding portion according to claim 48, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

22 37⁷². (Previously presented) The antigen-binding portion according to claim 49, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

38¹/₃. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 34 and a pharmaceutically acceptable carrier.

39¹/₄. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 35 and a pharmaceutically acceptable carrier.

40¹/₅. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 36 and a pharmaceutically acceptable carrier.

41¹/₆. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 37 and a pharmaceutically acceptable carrier.

42¹/₇. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 38 and a pharmaceutically acceptable carrier.

43¹/₈. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 39 and a pharmaceutically acceptable carrier.

44¹/₉. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 40 and a pharmaceutically acceptable carrier.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

~~45~~⁴⁶ 80. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~42~~⁹ and a pharmaceutically acceptable carrier.

~~46~~⁴⁷ 81. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~43~~¹⁰ and a pharmaceutically acceptable carrier.

~~47~~⁴⁸ 82. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~44~~¹¹ and a pharmaceutically acceptable carrier.

~~48~~⁴⁹ 83. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~45~~¹² and a pharmaceutically acceptable carrier.

~~49~~⁵⁰ 84. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~46~~¹³ and a pharmaceutically acceptable carrier.

~~50~~⁵¹ 85. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~47~~¹⁴ and a pharmaceutically acceptable carrier.

~~51~~⁵² 86. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~48~~¹⁵ and a pharmaceutically acceptable carrier.

~~52~~⁵³ 87. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~49~~¹⁶ and a pharmaceutically acceptable carrier.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

53 88. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 39 and a pharmaceutically acceptable carrier.

54 89. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 46 and a pharmaceutically acceptable carrier.

55 90. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 49 and a pharmaceutically acceptable carrier.

56 91. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 50 and a pharmaceutically acceptable carrier.

57 92. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 51 and a pharmaceutically acceptable carrier.

58 93. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 52 and a pharmaceutically acceptable carrier.

94. (Cancelled)

59 95. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 54 and a pharmaceutically acceptable carrier.

96. (Cancelled)

60 97. (Previously presented) The pharmaceutical composition according to claim 73, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

61 98. (Previously presented) The pharmaceutical composition according to claim 74, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

⁴⁰ 62 99. (Previously presented) The pharmaceutical composition according to claim ⁷⁵ 75, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴¹ 63 100. (Previously presented) The pharmaceutical composition according to claim ⁷⁶ 76, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴² 64 101. (Previously presented) The pharmaceutical composition according to claim ⁷⁷ 77, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴³ 65 102. (Previously presented) The pharmaceutical composition according to claim ⁷⁸ 78, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴⁴ 66 103. (Previously presented) The pharmaceutical composition according to claim ⁷⁹ 79, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴⁵ 67 104. (Previously presented) The pharmaceutical composition according to claim ⁸⁰ 80, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴⁶ 68 105. (Previously presented) The pharmaceutical composition according to claim ⁸¹ 81, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴⁷ 69 106. (Previously presented) The pharmaceutical composition according to claim ⁸² 82, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴⁸ 70 107. (Previously presented) The pharmaceutical composition according to claim ⁸³ 83, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

⁴⁹ 71 108. (Previously presented) The pharmaceutical composition according to claim ⁸⁴ 84, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

72 109. (Previously presented) The pharmaceutical composition according to claim ~~85~~⁸², further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

73 110. (Previously presented) The pharmaceutical composition according to claim ~~86~~⁸³, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

74 111. (Previously presented) The pharmaceutical composition according to claim ~~87~~⁸⁴, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

75 112. (Previously presented) The pharmaceutical composition according to claim ~~88~~⁸⁵, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

76 113. (Previously presented) The pharmaceutical composition according to claim ~~89~~⁸⁶, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

77 114. (Previously presented) The pharmaceutical composition according to claim ~~90~~⁸⁷, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

78 115. (Previously presented) The pharmaceutical composition according to claim ~~91~~⁸⁸, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

79 116. (Previously presented) The pharmaceutical composition according to claim ~~92~~⁸⁹, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

80 117. (Previously presented) The pharmaceutical composition according to claim ~~93~~⁹⁰, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

118. (Cancelled)

81 119. (Previously presented) The pharmaceutical composition according to claim ~~95~~⁹², further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

~~80~~ 120. (Previously presented) An isolated cell line that produces the antibody according to claim ~~134~~.

~~83~~ 121. (Previously presented) The cell line according to claim ~~120~~⁸² that produces antibody 2.13.2, or an antibody comprising the amino acid sequences of antibody 2.13.2.

~~88~~ 122. (Currently amended) A method for decreasing IGF-IR activation in a subject in need thereof comprising the step of administering to the subject an anti-IGF-IR antibody or ~~antigen-binding portion~~ according to claim ~~3934~~.

~~89~~ 123. (Currently amended) A method for increasing IGF-IR associated tyrosine phosphorylation in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or antigen-binding portion according to claim ~~3934~~.

~~90~~ 124. (Currently amended) A method for decreasing IGF-IR signaling in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or ~~antigen-binding portion~~ according to claim ~~3934~~.

~~91~~ 125. (Currently amended) A method for decreasing IGF-IR binding to IGF-I or IGF-II in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or ~~antigen-binding portion~~ according to claim ~~3934~~.

~~92~~ 126. (Currently amended) A method for decreasing the level of IGF-IR in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or antigen-binding portion according to claim ~~3934~~.

~~93~~ 127. (Currently amended) A method for inhibiting tumor growth in a subject in need thereof wherein said subject overexpresses IGF-I or IGF-IR, comprising

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

the step of administering to the subject an anti-IGF-IR antibody or antigen-binding portion according to claim ⁶¹3934.

⁹⁴ 128. (Previously presented) The method according to claim ⁹³127, wherein the tumor is a colorectal tumor.

⁹⁵ 129. (Previously presented) The method according to claim ⁹³127, wherein the tumor is a breast cancer tumor.

⁹⁶ 130. (Previously presented) The method according to claim ⁹³127, wherein the tumor is an epidermoid carcinoma cell tumor.

⁹⁷ 131. (Previously presented) The method according to claim ⁸⁷126, wherein the anti-neoplastic agent is adriamycin.

⁹⁸ 132. (Currently amended) A method of detecting the presence or location of an IGF-IR-expressing tumor in a subject in need thereof, comprising the steps of: ⁶

(a) administering the antibody according to any one of claims ¹³39, ¹⁸or ⁴⁶46 or ⁵¹51; and

(b) ~~detecting binding of said antibody, determining the expression of IGF-IR in the subject by localizing where the antibody has bound; and~~

(c) ~~diagnosing the presence or location of the tumor wherein said binding indicates the presence or [a] location of the tumor.~~

⁹⁹ 133. (Currently amended) A method of treating cancer in a human patient wherein said patient overexpresses IGF-I or IGF-IR, comprising the step of administering to the human patient an amount of the antibody according to claim ⁶¹39 or ¹³46 effective to treat said cancer.

¹⁰⁰ 134. (Currently amended) A method of treating a patient in need thereof with the antibody according to claim ⁶39, or ¹³46 or ¹⁸51, wherein said patient overexpresses

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

IGF-I or IGF-IR comprising the step of administering to the patient an effective amount of the antibody.

¹⁰⁰ 101 ¹³⁵ 135. (Currently amended) The method according to either of claims ⁹⁹ 133 or ¹³⁴ 134, further comprising the step of administering an anti-neoplastic, anti-tumor, anti-angiogenic or chemotherapeutic agent.

¹⁰² 136. (Previously presented) A method for decreasing IGF-IR activation in a subject in need thereof comprising the step of administering to the subject an anti-IGF-IR antibody according to claim ⁶ 39 or ¹³ 46.

¹⁰³ 137. (Previously presented) A method for increasing IGF-IR associated tyrosine phosphorylation in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim ⁶ 39 or ¹³ 46.

¹⁰⁴ 138. (Previously presented) A method for decreasing IGF-IR signaling in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim ⁶ 39 or ¹³ 46.

¹⁰⁵ 139. (Previously presented) A method for decreasing IGF-IR binding to IGF-I or IGF-II in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim ⁶ 39 or ¹³ 46.

¹⁰⁶ 140. (Previously presented) A method for decreasing the level of IGF-IR in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim ⁶ 39 or ¹³ 46.

¹⁰⁷ 141. (Currently amended) A method for inhibiting tumor growth in a subject in need thereof wherein said subject overexpresses IGF-I or IGF-IR, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim ³⁹ 39 or ⁴⁶ 46.¹³

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

¹⁰⁸142. (Previously presented) The method according to claim ¹⁰⁷141, wherein the tumor is a colorectal tumor.

¹⁰⁹143. (Previously presented) The method according to claim ¹⁰⁷141, wherein the tumor is a breast cancer tumor.

¹¹⁰144. (Previously presented) The method according to claim ¹⁰⁷141, wherein the tumor is an epidermoid carcinoma cell tumor.

¹¹¹145. (Previously presented) The method according to claim ¹⁰¹145, wherein the anti-neoplastic agent is adriamycin.

146. (Cancelled)

147. (Cancelled)

148. (Cancelled)

149. (Cancelled)

150. (Cancelled)

¹¹²151. (New) A monoclonal antibody that specifically binds insulin-like growth factor I receptor (IGF-IR) or an antigen-binding portion of said antibody, wherein the antibody or portion comprises the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in a heavy chain variable domain selected from the group consisting of:

(a) the variable domain of the heavy chain of antibody 2.13.2;

and

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

(b) the variable domain of a heavy chain comprising the amino acid sequence in SEQ ID NO: 8.

113 152. (New) The monoclonal antibody or antigen-binding portion according to claim 151, wherein said antibody is selected from the group consisting of: an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, a single chain antibody or a bispecific antibody.

114 153. (New) The antigen-binding portion according to claim 151, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

115 154. (New) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 151 and a pharmaceutically acceptable carrier.

116 155. (New) The pharmaceutical composition according to claim 151, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

117 156. (New) An isolated cell line that produces the antibody according to claim 151.

118 157. (New) The monoclonal antibody or antigen-binding portion thereof according to claim 154, wherein the heavy chain amino acid sequence further utilizes a human D6-19 gene and a human JH6 gene.

119 158. (New) The monoclonal antibody or antigen-binding portion according to claim 156, wherein the light chain amino acid sequence further utilizes a human Jk1 gene.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

120 159. (New) A method of detecting the presence or location of an IGF-IR expressing tumor in a subject, comprising the steps of:

- a) administering the antibody according to claim 21/160 to the subject; and
- b) detecting binding of said antibody, wherein said binding indicates the presence or location of the tumor.

121 160. (New) A monoclonal antibody that specifically binds insulin-like growth factor I receptor (IGF-IR) or an antigen-binding portion of said antibody, wherein the antibody or portion comprises the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in the variable domain of a light chain comprising SEQ ID NO: 6 and the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in the variable domain of a heavy chain comprising SEQ ID NO: 8.

122 161. (New) The monoclonal antibody or antigen-binding portion according to claim 121/160, wherein said antibody is selected from the group consisting of: an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, a single chain antibody or a bispecific antibody.

123 162. (New) The antigen-binding portion according to claim 121/160, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')₂ fragment and an Fv fragment.

124 163. (New) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 121/160 and a pharmaceutically acceptable carrier.

125 164. (New) The pharmaceutical composition according to claim 121/160, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

12/ 126 165. (New) An isolated cell line that produces the antibody according to claim 160.

127 166. (New) The method according to claim 85/ 24, further comprising the step of administering at least one additional chemotherapeutic agent.

128 167. (New) The method according to claim 85/ 24, wherein said method further comprises radiotherapy.

129 168. (New) The method according to claim 99/ 133, further comprising the step of administering at least one additional chemotherapeutic agent.

130 169. (New) The method according to claim 99/ 133, wherein said method further comprises radiotherapy.